REMARKS/ARGUMENTS

I. Status of the Claims and Amendments:

Claims 145 – 146, 149, 162 and 169 have been cancelled in light of current amendments. The remaining claims 144, 147 – 148, 150 - 161, 163 – 168 and 170 – 192 remain pending in the application.

II. Rejections under 35 U.S.C. §112 Written Description

The Examiner has asserted a written description rejection as it relates to "possession of the invention." In the interests of advancing prosecution and without prejudice as to the potential to pursue claims of varying scope in further related applications, all claims in the present application have been amended to claim molecular switches utilizing the ligand binding domain of the progesterone hormone receptor, thus a single species of the family of steroid hormone receptors. To the extent that the present written description rejection relates to a scope encompassing all steroid hormone receptors, the present rejection would appear to be obviated. Furthermore, all pending claims have been amended to provide that the mutation is in one or more of the C' terminal amino acids of the ligand binding domain. As exemplified by the specific examples provided, including data and figures, it is absolutely clear to those of skill in the art that the inventors had possession of the presently claimed invention relating to molecular switches utilizing a mutated progesterone hormone receptor and in particular, where the mutation is in one or more of the C' terminal amino acids of the ligand binding domain.

Any further requirement that the claims be limited to specific disclosed embodiments is respectfully traversed as discussed in more detail below.

III. Rejections under 35 U.S.C. §112 – Scope of Enablement

The Examiner has argued that the specification is not enabling for the generation of any mutation in the ligand binding domain of any steroid hormone receptor. While not acquiescing to the Examiner's apparent basis of rejection, and reserving the future right to pursue claims of different scope, in the interests of advancing prosecution of the present case, all independent claims, thus the claims dependent therefrom, have been amended to recite that the ligand binding

domain is a mutated progesterone receptor ligand binding domain and that the mutation is in one or more of the C' terminal amino acids of the ligand binding domain. As two examples of this, the specification at page 29, lines 10 – 30 provides specific examples of both 54 and 42 amino acid deletions that are able to provide the remarkable change in ligand specificity. Given this teaching, undue experimentation would not be required to identify further deletions or substitutions in this region that would provide the same result as the surprising discovery of the present inventors that modification of amino acid sequence in this region would convert an antagonist of the naturally occurring receptor into an antagonist. It is respectfully submitted that given the level of skill in the art, the claimed scope is fully enabled and to require the applicants to further narrow the scope is not justified under the enablement standard.

Applicant appreciates the Examiner's finding that the specification is enabling for transgenic applications where the animal expresses the molecular switch. In the interests of advancing prosecution, claim 144 and the claims that depend therefrom are amended to recite a method in which the molecular switch is expressed in the non-human transgenic animal. The expression from the target gene, however, is regulated and thus, whether the target gene is endogenous or introduced, its expression will not be changed until the expressed molecular switch is converted to active form by the action of the ligand. Although not conceding that the prior claims lacked clarity on this point, independent claims 168 and 177 have been similarly amended to recite that the molecular switch is expressed.

Claims 168 and 177 have been amended to recited "transient expression" but only as distinguished from the type of long term expression such as is found for the lifetime of an animal as in transgenic applications. As previously explained, where the nucleic acids have been administered to an animal using an expression vector, expression is expected to be "transient" in that the expression vector will eventually be lost to cell division. Nonetheless, "transient" expression can still persist for prolonged periods of time as reflected by the previously submitted article by Nordstrom, *Steroids* 68 (2003) 1085-1094, pg. 1091, in which ligand inducible expression of target genes under the present method has been observed for at least a year following single administration of expression vectors encoding the molecular switch of the present invention. It is respectfully submitted that the focus of the claims is a method of regulating expression of

genes using the molecular switch for however long the encoded molecular switch and the target gene persist in the cell.

IV. Rejections under 35 U.S.C. §112 ¶2.

Claims 168 – 176 were rejected under §112, 2nd paragraph, on the grounds that it was unclear as to whether the ligand and the molecular switch expression vector are located in the same animal. Independent claim 168 as presently amended clearly recites the ligand is administered to animal that had been previously administered a molecular switch expression cassette.

Conclusion

For the reasons stated herein, the Applicant respectfully submits that independent claims 144, 168 and 177 are allowable and that the dependent claims are, in turn, also allowable. Applicant respectfully requests allowance of the claims at an early date. The Commissioner is authorized to charge any additional fees incurred in this application or credit any overpayment to Deposit Account No. 50-1922. Should the Examiner have any questions, please do not hesitate to call Applicant's attorney at 832-446-2421.

Respectfully submitted,

By _____

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